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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/602,489	06/23/2003	Ian David Manger	020174-008620US	1122

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EXAMINER
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HYUN, PAUL SANG HWA

ART UNIT	PAPER NUMBER
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1797

MAIL DATE	DELIVERY MODE
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11/25/2009

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/602,489	<b>Applicant(s)</b> MANGER ET AL.	
	<b>Examiner</b> PAUL S. HYUN	<b>Art Unit</b> 1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 13 July 2009.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-15 and 18-40 is/are pending in the application.
- 4a) Of the above claim(s) 1-13, 32 and 33 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 14, 15, 18-31 and 34-40 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 13 July 2009 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                    | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

### DETAILED ACTION

The amendment filed by Applicant on July 13, 2009 has been acknowledged. Claims 1-15 and 18-40 are currently pending wherein claims 1-13, 32 and 33 remain withdrawn pursuant to a restriction requirement. Applicant amended claims 14, 22, 34 and 38.

The amended drawings filed by Applicant has been acknowledged.

Despite the amendment, the rejections are maintained.

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims **14, 15, 18-26, 28-31 and 34-40** are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Dam et al. (US 2003/0008411 A1) in view of Quake et al. (US 2002/0037499 A1).

Van Dam et al. disclose a microfluidic device and a method for synthesizing a library of compounds by using the microfluidic device (see claim 15), which includes DNA synthesis (see [0056]). The device comprises a solid substrate layer and an elastomeric layer attached to the solid substrate wherein the surface of the solid substrate is immobilized with ligands for binding analytes of interest. The surfaces of both layers can comprise grooves/wells to define a plurality of first flow channels

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intersecting a plurality of second flow channels (see claim 24 and [0048]). The device further comprises a plurality of control channels associated with each of the flow channels. Each control channel comprises a chamber delimited by an elastic membrane. Upon the application of an actuation force within a control channel, the elastic membrane of the control channel deflects into the flow channel to block fluid flow through the flow channel. The control channels also act as a pump when they are actuated sequentially to facilitate the flow of fluids through the flow channels (see [0068] and [0069]). Because the control channels can be sequentially actuated, it is apparent that the control channels can be independently actuated with respect to other control channels.

The method disclosed by the reference comprises the steps of:

- manipulating the control valves to restrict flow in the second flow channels,
- introducing a reagent into the first flow channels such that the reagent binds to the ligands immobilized to the surface of the solid substrate, and
- introducing a sample solution into the second flow channels such that the sample in the sample solution circulates through the flow channels and binds the reagents bound to the immobilized ligands (see claims 25 and 26).

The reference discloses that the term “reagent” refers to oligonucleotides, peptides, monomers, and other small molecules that are building blocks of a larger molecule (see [0056]). While the fluid is being introduced into one of the two flow channels, the other set of flow channels is closed off by means of the control valves in order to prevent cross-contamination (see [0089]). The reference also discloses that

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reagents/samples that do not bind to the substrate are rinsed off using a solvent (see [0084]). The efficacy of the binding is accomplished by reacting the immobilized ligands with fluorophores and detecting the fluorescence (see [0122]). The method disclosed by Van Dam et al. differs from the claimed method in that Van Dam et al. do not disclose the step of manipulating the valves to form a closed loop.

Quake et al. disclose a microfluidic device similar to the device disclosed by Van Dam et al. Like the device disclosed by Van Dam et al., the device comprises intersecting microfluidic channels and elastomeric valves. Quake et al. also disclose a method for detecting analytes, the method comprising the steps of hybridizing a sample with probes immobilized to the surface of the microfluidic channels. Quake et al. also disclose the step of manipulating the valves to form a closed loop of flow channels. The closed loop enables the sample to circulate throughout the loop and properly hybridize with the probes (see Abstract and [0076]). Quake et al. also disclose the step of incubating the reaction to enable proper hybridization (see [0310]). In light of the disclosure of Quake et al., it would have been obvious to one of ordinary skill in the art to manipulate the valves of the Van Dam et al. device to form a closed loop of channels during the hybridization step to ensure that the sample and the reagents properly hybridize. It also would have been obvious to incubate the reaction to ensure proper hybridization. Naturally, if one were to form a closed loop of flow channels within the Van Dam et al. device, the closed loop would span multiple rows and columns of channels. Likewise, because the closed loop would span multiple rows and columns, at

least two control lines (one for manipulating the x-axis valves and another for manipulating the y-axis valves) would have to be actuated to form the closed loop.

With respect to claims 23-26, Van Dam et al. disclose the step of derivatizing the solid substrate and determining the efficacy of the derivatization (see [0122]). This is accomplished by reacting the immobilized ligands with fluorophores and detecting the fluorescence. In light of the disclosure, it would have been obvious to one of ordinary skill in the art to tag the synthesized compounds produced by the method described above and detect the fluorescence using a fluorescent microscope in order to observe the efficacy of the synthesis.

With respect to claim 31, given that the device disclosed by Van Dam et al. is adapted to perform binding assays, it would have been obvious to one of ordinary skill in the art to react any two entities that bind using the device disclosed by Van Dam et al., including a cell as the reagent and antimicrobes as the sample in order to observe the effects of the antimicrobes on the cell.

Claim **27** is rejected under 35 U.S.C. 103(a) as being unpatentable over Van Dam et al. in view of Quake et al. as applied to claims 14, 15, 18-26, 28-31 and 34-37, and further in view of Raillard et al. (US 2002/0102577 A1).

Van Dam et al. does not explicitly disclose the usage of a non-optical detector to observe the compound synthesis.

Raillard et al. disclose a method for labeling probes with radio-isotopes that emit radiation (see [0132]). The probe is detected using a detector that is sensitive to radiation.

In light of the disclosure of Raillard et al., it would have been obvious to one of ordinary skill in the art to tag the synthesized compounds produced by the method disclosed by Van Dam et al. with radio-isotope probes instead of fluorophores and detect the radiation using a radiation detector in order to observe the efficacy of the synthesis in the event that fluorophores are not available.

### ***Response to Arguments***

Before addressing Applicant's arguments, it should be noted that the distinctions between Applicant's invention and the invention disclosed by Van Dam et al. articulated by Applicant in the interview conducted on July 9, 2009 have been fully considered. However, the amendment filed by Applicant does not sufficiently distinguish Applicant's invention from the invention disclosed by Van Dam et al.

Applicant's arguments with respect to the claims have been fully considered but they are not persuasive.

1) Applicant argues that claims 14, 15, 18-31 and 38 are patentable over the prior art because neither Van Dam et al. nor Quake et al. disclose the step of applying an actuating force from two control lines to a plurality of sets of closed loop forming control valves to form a plurality of closed looped flow channels such that each closed looped flow channel spans multiple rows and columns. This argument is not persuasive because the cited references, in combination, teach the limitation in question. At the

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very least, the references provide the motivation to conduct the step of applying an actuating force from two control lines to a plurality of sets of closed loop forming control valves to form a plurality of closed looped flow channels such that each closed looped flow channel spans multiple rows and columns.

Van Dam et al. disclose flowing fluid in a serpentine manner through the disclosed device (see [0190]). The disclosure suggests that fluid flow through the device is not limited to a single row channel or column channel. In addition, the disclosure suggests that the device is capable of forming a looped flow channel by manipulating the valves situated at the terminus of each row and column. The Quake et al. reference was relied upon for its disclosure of manipulating valves in a microfluidic device to form a closed loop of flow channels. The closed loop enables a sample to circulate through a channel multiple times and properly hybridize with reagents (see Abstract and [0076]). Given that the disclosure of Van Dam et al. is also directed towards conducting hybridization reactions, there is motivation to form a closed loop of flow channels within the Van Dam et al. device by manipulating valves as taught by Quake et al. Naturally, if one were to form a closed loop of flow channels within the Van Dam et al. device, the closed loop would span multiple rows and columns of channels. Likewise, because the closed loop would span multiple rows and columns, at least two control lines (one for manipulating the x-axis valves and another for manipulating the y-axis valves) would have to be actuated to form the closed loop. For the foregoing reason, Applicant's argument with respect to claims 14, 15, 18-31 and 38 is not persuasive.



2) Applicant argues that claims 34-37, 39 and 40 are patentable over the prior art because neither Van Dam et al. nor Quake et al. disclose a first loop forming control valve actuated by a first control line or a second loop forming control valve actuated by a second control line. This argument is not persuasive because Van Dam et al. disclose such control valves actuated by control lines. Van Dam et al. disclose control line 320 that provides pressure to the valves that control flow through the columnar channels, and control line 324 that provides pressure to the valves that control flow through the horizontal channels (see Fig. 5). The Examiner maintains the position that the arrangement illustrated in figure 5 of Van dam et al. is within the scope of the limitation in question. For the foregoing reason, Applicant's arguments with respect to claims 34-37, 39 and 40 is not persuasive.

### ***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL S. HYUN whose telephone number is (571)272-8559. The examiner can normally be reached on Monday-Friday 8AM-4:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jill Warden can be reached on (571)-272-1267. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Paul S Hyun/  
Examiner, Art Unit 1797

/Jill Warden/  
Supervisory Patent Examiner, Art Unit 1797